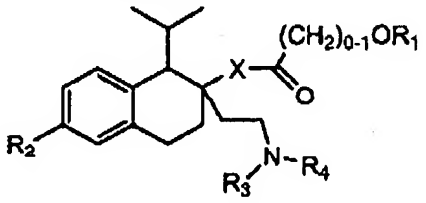
REMARKS

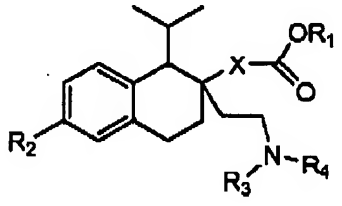
Claim 22 has been canceled without prejudice to future prosecution. Claims 23 and 24 have been amended to convert them from dependent claims to independent claims. The dependencies of claims 32 and 33 have been amended in view of the cancellation of claim 22. Claim 23 has been amended to remove one of the moieties in the definition of R_{10}.

New claim 34 has been added. Claim 34 is substantially identical to claim 23 except that:

a) the structure of the recited compound is



in new claim 34 rather than



and

b) R_{15} is defined as H in new claim 34.

Support for inclusion of the $(CH_2)_{0-1}$ moiety is found in claims 3, 6-11, 24 and 26-31 as originally filed and Figures 10-12 of the specification. Support for R_{16} being H is found in claims 3-7, 9, 24-27 and 29 as originally filed and in Figs. 10 and 11, which all display compounds having benzimidazole moieties in which R_{15} is H. No new matter has been added by way of these amendments.

I. Discussion of the Rejection under 35 U.S.C. § 112, First Paragraph

Claims 22, 32 and 33 have been rejected under 35 U.S.C. § 112, first paragraph, for lacking enablement. Claim 22 has been canceled and the dependencies of claims 32, and 33 amended to refer to claim 23. Consequently, this rejection is obviated.

Claims 22, 23-29, 32 and 33 also have been rejected under 35 U.S.C. § 112, first paragraph, for lacking enablement. Specifically with regard to claims 23-29, it appears the Office alleges that these claims lack enablement because no working examples have been provided. On pages 7-8, points 1-4, the Office alleges that the claims comprise hundreds of compounds but the specification provides no working examples or tests demonstrating calcium channel blocking activity. However, the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to

practice it without an undue amount of experimentation. In re Borkowski, 422 F.2d 904, (CCPA 1970); M.P.E.P. § 2164.02.

In point 5 on page 8 of the Office Action, the Office states:

1. pharmacological activity is generally a highly unpredictable area.
2. mibefradil, of which the presently claimed compounds are analogs, was removed from the market due to drug-drug interactions.
3. the claimed invention is highly unpredictable because the enzymatic hydrolysis of the soft calcium channel blockers results in metabolites with acidic functional groups (which have high solubility) and having different functional groups result in different biological properties such as drug-drug interactions, formation of toxic metabolites or increased and longer exposure to the parent compound etc. .

With regard to item 1, while pharmacological activity may generally be unpredictable, the compounds recited in the present application are not simply random molecules for which pharmacological acitivity is asserted. Quite to the contrary. The compounds of the present claims are analogs of a known calcium channel blocker and, furthermore, were specifically designed to a) maintain the calcium channel blocking activity of mibefradil and b) decrease the toxicity of mibefradil:

> Specifically, in a preferred embodiment, the therapeutic compounds of the subject invention contain an ester group, which does not detract from the ability of these compounds to provide a therapeutic benefit, but which makes these compounds more susceptible to degradation by hydrolysis, particularly serum and/or cytosolic esterases.

Specification p. 8, ll. 12-16. Furthermore, the compounds of the present claims are the same as or analogs of the compounds of Figs. 1-9, which the Office acknowledged at page 2 of the present Office Action are enabled for blocking calcium channels. It is respectfully submitted, therefore, that given the similarity of the present compounds to the known calcium channel blocker mibefradil as well as compounds in Figs. 1-9 that the Office has acknowledged are enabled and the forethought the inventors instituted in design the compounds of the present claims, one of ordinary skill in the art would have a reasonable expectation that the recited compounds would inhibit calcium channel activity in a patient as claimed.

With regard to items 2 and 3 (above), the applicants respectfully submit that toxicity is irrelevant to whether the claims are enabled for the recited method of blocking calcium channels in a patient. The issue is whether one of ordinary skill in the art could, without undue experimentation, block calcium channels in a patient by administering the recited compounds. As explained immediately above, one of skill in the art would reasonably expect the recited compounds to block calcium channels. Safety is an issue for the FDA, not the Patent Office. *See, e.g.*, MPEP 2701.01, parts III and IV.

Furthermore, as explained in the specification, the present compounds were designed for improved safety, and the Office has supplied only generalized and unsubstantiated assertions regarding the recited molecules that neither address nor rebut the specific teachings of the specification regarding decreased toxicity.

Lastly, in point 7 on p. 9 of the Office Action, the Office alleges:

> In order to practice the claimed invention, one of ordinary skill in the art would have to first envision a specific soft calcium channel blocking compound of the instant invention for the treatment, a dosage for each compound, the duration of treatment, route of treatment etc.

and that this would require undue experimentation. The applicants respectfully disagree. Selecting a compound of the present claims is a simple matter as the structures are well defined. Furthermore, determining dosage and duration and route of treatment may take some work, but it is nevertheless merely routine and, therefore, not "undue," as one of ordinary skill in the art would recognize that such work would be essentially identical to the work conducted for previously identified and tested calcium channel blockers.

In conclusion, the applicants respectfully submit that given the structural analogy of the presently recited compounds to known calcium channel blockers and compounds the Office has acknowledge are enabled (Figs. 1-9) as well as the rationale developed by the applicants for their design of these molecules, the applicants respectfully submit that it would be a routine matter for one or ordinary skill in the art to administer the recited compounds to a patient in need of calcium channel blocking to achieve such blocking. Accordingly, the applicants respectfully request that the 35 U.S.C. § 112, first paragraph, rejections be reconsidered and withdrawn.

II **Discussion of the Rejection under 35 U.S.C. § 112, Second Paragraph**

Claims 24-27 and 29 have been rejected under 35 U.S.C. § 112, second paragraph, for allegedly lacking antecedent basis. With the amendment to claim 24 making it independent this rejection is obviated.

III **Discussion of the 35 U.S.C. § 102(b) Rejection**

Claims 22, 32 and 33 have been rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Branca et al. (U.S. Pat. No. 4,808,605). Claim 22 has been canceled and claims 32 and 33 amended to depend from claim 23, thereby obviating this amendment.

CONCLUSION

In view of the above remarks, the application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of this application, the Examiner is invited to call the undersigned attorney. If the Examiner has any questions regarding this amendment, the Examiner is invited to call the undersigned at (312) 913-2135.

Respectfully submitted,
McDonnell Boehnen Hulbert & Berghoff LLP

Dated: May 6, 2005

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